

**AMENDMENTS TO THE SPECIFICATION**

**IN THE SPECIFICATION:**

**Page 2**

Please amend the Specification on page 2 beginning at line 3 as follows:

The  $\alpha_4\beta_1$  integrin, also known as VLA-4 (Very Late Antigen-4), is constitutively expressed on the surface of leukocytes including lymphocytes, monocytes, eosinophils and basophils (see Hemler et al., *J. Bio. Chem.* 262:11478-11485 (1987); and Bochner et al., *J. Exp. Med.* 173:1553-1556 (1991)). VLA-4 is reported to be present on neutrophils from septic patients (see Ibbotson et al., *Nature Med.* 7:465-470 (2001)). VLA-4 binds to vascular cell adhesion molecule-1 (VCAM-1) on activated endothelial cells, resulting in extravasation of leukocytes (Elices et al., *Cell* 60:577-584 (1990)). Once the cells have reached the extravascular space, VLA-4 can bind to the connecting segment 1 (CS-1), an alternatively spliced region of the FN A chain (~~Wayne~~ Wayner et al., *J. Cell Biol.* 109:1321-1330 (1989)). In addition, VLA-4 is known to bind to osteopontin, a protein upregulated in arteriosclerotic plaques (see Bayless et al., *J. Cell Science* 111:1165-1174 (1998)).

**Page 14**

Please amend the Specification on page 14 beginning at line 20 as follows:

The Jurkat J6 Scintillation Proximity Assay was used to investigate the interaction of the integrin VLA-4 expressed on the Jurkat J6 cell membrane with test compounds. J6 cells (1 million cells/well) were allowed to coat wheat germ agglutinin coated SPA beads (Amersham,

1mg/well) in assay buffer containing 50mM HEPES, 100mM NaCl and 1mM MnCl<sub>2</sub> (pH adjusted to 7.5 with 4M NaOH). Tritiated <sup>3</sup>H Standard Compound A (1-3 nM final assay concentration) and test compounds were dissolved in an appropriate solvent and diluted in assay buffer (the top assay concentration being ~~2.5µm~~ 2.5µM; ten point dose response curve).

Compounds were assayed in duplicate, a four parameter curve fit being applied. The equilibrium dissociation constant for each compound was calculated according to the method of Cheng & Prusoff (Biochem Pharmacol., 22(23) : 3099 - 3108 (1973)). Data were presented as the mean pKi.

#### Page 34

Please amend the Specification on page 34 beginning at line 25 continuing onto page 35 as follows:

#### **(R)-(-)-3-(4-Hydroxymethylphenyl)pentanoic acid methyl ester (P29)**

A solution of (R)-3-(4-hydroxymethylphenyl)pentanoic acid (P27, 2.0 g, 9.6 mmol) in methanol (150 mL) and concentrated sulfuric acid (3 mL) was heated at reflux for 1.5 hours and then cooled, concentrated under reduced pressure and partitioned between ethyl acetate (100 mL) and water (100 mL). The aqueous layer was further extracted with ethyl acetate (2x50 mL) and the combined organic layers washed with brine (50 mL), dried over anhydrous magnesium sulfate, filtered and evaporated to dryness. After purification by column chromatography on silica gel with 1:1 ethyl acetate: hexane as eluent the title compound was obtained as a colourless oil; MS (ES+ve): [M-OH]<sup>+</sup> at m/z 205 (C<sub>13</sub>H<sub>18</sub>O<sub>3</sub> requires [M-OH]<sup>+</sup> at m/z 205); [α]<sub>D</sub><sup>30°C</sup> -30.7° (c = 1.0, MeOH).